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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/830,810 | 07/25/2001 | Martin M. Matzuk | P01925US1 | 2015 |

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| EXAMINER | |
|---|---|
| DESAI, ANAND U | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1653 | |

DATE MAILED: 10/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/830,810 | MATZUK ET AL. | |
| | Examiner | Art Unit | |
| | Anand U Desai, Ph.D. | 1653 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2-10 and 58-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-10 and 58-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/8/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. This office action is in response to Amendment filed on July 21, 2004. Claims 1, and 11-57 have been cancelled. New claims 58-61 have been added. Claims 2-10, and 58-61 are currently pending and are under examination.

**Maintenance of Rejections**

### *Claim Objections*

2. Claim 2 is objected to because of the following informalities: The claim would be clearer if written to claim the disclosed sequence instead of a figure. Suggest, An isolated polynucleotide having the polynucleotide sequence set forth in SEQ ID NO:1. Appropriate correction is required.

### *Double Patenting*

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 2-4, and 58-61 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, and 2 of copending Application No. 10/475,502. Although the conflicting claims are not identical, they are not

patentably distinct from each other because the current application claims an isolated polynucleotide sequence, O1-180, identified as SEQ ID NO:1 that is isolated from a mammalian cell, and copending Application No. 10/475,502 claims an isolated polynucleotide sequence encoding O1-180, identified as SEQ ID NO:11, and 13.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Claim Rejections - 35 USC § 101***

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 2-10, and 58-61 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The claims are directed to an isolated polynucleotide sequence designated as SEQ ID. NO: 1. The specification does not specifically address the activity or use of the polynucleotide, SEQ ID. NO: 1. On page 2, line 30 the polynucleotide is suggested to function as other oocyte specific genes. On page 3, starting at line 4 of the specification the polynucleotide is described in a general manner to relate to various cell proliferative or degenerative disorders, and infertility. On page 3, beginning on line 16, the specification describes the use of the polynucleotide as a reagent to study ovarian development and function. The specification also discloses that the polynucleotide can be used to screen for genetic mutations in components of signaling pathways that are associated with some forms of human infertility or gynecological cancers. On page 3, beginning on line 25 the polynucleotide is suggested to be used in the generation of mutant mice

for the further study of oogenesis and/or folliculogenesis. The knockouts are suggested to provide key insights into the roles of the polynucleotide gene product in human female reproduction. On page 7, beginning on line 1, the specification states that based on the known activities of many other ovary specific proteins, it can be expected that the protein product from the polynucleotide will also possess biological activities that will make them useful as diagnostic and therapeutic reagents. On page 7, beginning on line 5, the specification suggests that based on similar expression patterns of the claimed novel polynucleotide and a growth differentiation factor-9, the protein product of the polynucleotide would function in a similar manner. On page 7, beginning on line 14, the specification suggests that since the protein product of the polynucleotide has similar tissue of origin as inhibin, both would possess similar biological activities. On page 7, line 23, the specification discloses that the protein of the polynucleotide may be useful as an indicator in prenatal screening procedures. On page 7, beginning on line 25, the specification suggests that the protein of the polynucleotide may function for the treatment of ovarian cancer. On page 19, beginning on line 2, the specification suggests that sequences complementary to the polynucleotide sequence claimed could be used in treatments of cell-proliferative disorders. On page 20, line 5, the specification teaches the use of the polynucleotide in gene therapy. On page 23, line 15, the specification states that the protein product of the polynucleotide could play a role in regulation of the menstrual cycle, and therefore, could be useful in various contraceptive regimens. On page 28, beginning on line 18, the specification discloses that the open reading frame of the polynucleotide product fails to demonstrate any structural motifs reminiscent of known proteins, suggesting that they will be functionally unique. These are not considered to be specific or substantial utilities for the

polynucleotide. The method such as recombinant production of protein is not considered to be specific or substantial utility. These asserted utilities are broad and are not specific to the polynucleotide of SEQ ID. NO: 1. There is no disclosed signaling pathway associated with the polynucleotide of SEQ ID. NO: 1, and there is no disease or disorder correlated with the polynucleotide of SEQ ID. NO: 1. For example, on page 19, the passage does not disclose which cell-proliferative disorders will be treated with the polynucleotide of SEQ ID. NO: 1. Given that the specification does not disclose how to use the polynucleotide, a skilled artisan would not know how to use the polynucleotide or a polynucleotide that hybridizes with it. Thus, the specification fails to set forth a specific and substantial utility.

***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2-10, and 58-61 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 4, 58-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. In claim 4, which depends ultimately from claim 2, appears to be directed to an isolated polynucleotide from a mouse. Is the sequence identified as SEQ ID NO:1 in a rat, pig, cow or human cell?

10. The term "specifically hybridizes" in claims 58 and 60 is a relative term, which renders the claim indefinite. The term "isolated polynucleotide" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. What are the conditions, the temperature, and concentration of salt in hybridization buffer, for a polynucleotide that specifically hybridizes?

11. Claims 59, and 61 are rejected for depending on a rejected claim.

**Response to Applicant's Remarks**

Applicants traverse the rejections of claims 2-10 under 35 USC § 102, and § 112. Applicants state the Patent Office did not properly establish a *prima facie* case of lacking utility. Applicants state that the specification defines SEQ ID NO:1 as an ovary specific polynucleotide, and thus one of skill in the art would understand that any cell proliferative disorder or disease associated with SEQ ID NO:1 would be related to an ovary type disease or disorder, such

diseases include ovarian tumors, including germ cell tumors, and granulose cell tumors, infertility, such as premature ovarian failure. Applicant further states that expression of SEQ ID NO:1 is similar to that of GDF-9, which is known to play a role in fertility. Applicants state that the specification describes blocking the expression of SEQ ID NO:1 would result in a contraceptive action. Applicants state that mRNA encoded by SEQ ID NO:1 is specific to the oocytes, and thus one skilled in the art would know that this polynucleotide and products thereof would play a role in oogenesis or folliculogenesis, more specifically fertility. Applicants further assert a specific utility by submitting a declaration by one of the inventors, as well as a manuscript published online on January 21, 2003 in Nature Genetics.

Applicant's remarks and declaration under 37 CFR 1.132 filed on July 21, 2004 have been thoroughly reviewed and considered, but is insufficient to overcome the rejection of claims 2-10 based upon lack of utility and/or inoperativeness under 35 U.S.C. 101 and 112, 1st paragraph as set forth in the last Office action because they are not found persuasive for the following reasons:

The 35 U.S.C. 101 rejection clearly sets forth the reasoning used in concluding that the asserted utility for the claimed invention is neither specific and substantial or a well established utility. The method such as recombinant production of protein is not considered to be specific or substantial utility. These asserted utilities are broad and are not specific to the polynucleotide of SEQ ID. NO: 1. The suggestion that a similar expression pattern confers similar function is not convincing. There is no disclosed signaling pathway associated with the polynucleotide of SEQ ID. NO: 1, and there is no disease or disorder correlated with the polynucleotide of SEQ ID. NO: 1. Just because one gene such as GDF-9 plays a role in fertility does not mean that any oocyte

specific gene will play a role in fertility. In addition, example 7 in the specification appears to describe further research that can be performed to identify a function of the protein encoded by the isolated polynucleotide of SEQ ID NO:1.

Further, the publication submitted in support of a specific and substantial or a well established utility, which was published in January of 2003 states that human ZAR1 is transcribed in the ovary and testis, thus not ovary specific (see pg. 188, 2nd paragraph, left column), and that a PHD motif found in ZAR1 and Zar1 (O1-180, SEQ ID NO:1) may confer a transcriptional regulator activity to the protein, which demonstrates the function of the protein is still unknown. The manuscript suggests that $Zar1^{-/-}$ mice arrest at the two-cell embryo stage, but the mechanism has yet to be determined (see pg. 189-190). On page 190 of the manuscript the authors state that identification of proteins that interact with Zar1 may provide insights into the role of Zar1 (SEQ ID NO:1) in regulating the transition from oocyte to embryo, which is indicative of further experimentation for characterization of a protein encoded by the isolated polynucleotide identified as SEQ ID NO:1. Thus, the specification still fails to set forth a specific and substantial utility.

***Conclusion***

12. No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

October 6, 2004

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER